FINAL
CLINICAL TRIALS MONITORING SERVICE

CANCER CENTER VISIT SUMMARY

Site Visit Date:	**Date of Last Site Visit:**	**Institution/City:**	**Cancer Center Director:**
xxxx 00-00, 2002	xxxx 00-00, 1999	Somewhere University Hospital	John Bull, Ph.D.

Institution Staff:	**Title:**	**Audit Team/Institution:**
xxxxxxxxxxxxxxxx, M.D.	Investigator	xxxxxxxxxxxxxxx Pharm.D. / CTMS
xxxxxxxxxxxxxxxx, M.D.	Investigator	xxxxxxxxxxx, M.D. / NIH
xxxxxxxxxxxx, M.D.	IRB Chair	xxxxxxxxxx, M.G.A./ NCI
xxxxxxxxxxx, R.N.	Associate Director, Clinical Investigations Support Office	xxxxxxxxxxxxxx, B.S. / NCI
xxxxxxxxxxx, Pharm.D.	Research and Drug Information Coordinator	xxxxxxxxxxxx, R.N. / CTMS
xxxxxxxxxxxxx	Data Manager	xxxxxxxxxx, R.N., OCN®, CCRA / CTMS
xxxxxxxxxxxxx, M.D.	Director, Clinical Investigations Support Office	xxxxxxxxxxxxxxx, M.P.H. / CTMS
xxxxxxxxx	Data Manager	
xxxxxxxxxxxxxxx, R.N.	Research Nurse	
xxxxxxxxxxxxx	Data Manager	
xxxxxxxxxxxxxx	Data Manager	
xxxxxxxxxxxxx	Data Manager	
xxxxxxxxxxxxxxx	Data Manager	
xxxxxxxxxxxxxx, R.N.	Research Nurse	
xxxxxxxxxxxxxxxxxx, MPH	Project Manager, Clinical Investigations Support Office	

PROTOCOLS REVIEWED

Protocol #	**Protocol Chair**	**IND Drugs/Other Modalities**	**Disease**
zzzzzzzz	zzzzzzzzzzzzzzzz, MD	zzzzzzzzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzz
zzzzzzzz	zzzzzzzzzzzzzzzz, MD	zzzzzzzzzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzz
zzzzzzzz	zzzzzzzzzzzzzzzz, MD	zzzzzzzzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzzzzzzzzzzzzzzz
zzzzzzzz	zzzzzzzzzzzzzzzz, MD	zzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzzzzzzzzzzzzzzzz
zzzzzzzz	zzzzzzzzzzzzzzzz, M.D.	zzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzz
zzzzzzzz	zzzzzzzzzzzzzzzz, M.D.	zzzzzzzzzzzzzzzzzzzzzzz	zzzzzzzzzzzzzzzzzzzzzzzzzzzzz

1. INSTITUTIONAL REVIEW BOARD/INFORMED CONSENT

A. Were all protocols IRB approved prior to the entry of the first patient?

B. Were all yearly reapprovals and amendment reviews conducted on time?

The institution establishes the date of continuing review at the time of the original review. The date remains fixed regardless of when the continuing review is conducted. Occasionally the continuing review was done 6 weeks before the due date. The site recently became aware of the Office of Human Research Protections July 11, 2002 Guidance on Continuing Review. The Guidance directs institutions that the due date can remain the same if the review is done within four weeks. If done earlier, the due date is to be revised. Expedited adverse events were not always submitted to the NCI and IRB in a timely manner. It also appears that the internal form and the AdEERs report are not always completed at the same time.

C. Do the informed consents contain all required elements and are the risks/benefits analogous to that listed in the NCI approved model informed consent?

2. DRUG ACCOUNTABILITY

A. NCI Drug Accountability Record Forms (NCI DARFs)

1. Completely and correctly filled out
2. Protocol and drug specific
3. Satellite records accounted for
4. NCI DARFs kept as primary transaction record
5. Balance on NCI DARFs (protocols/agents) matches shelf count
6. Patients cross-checked with NCI DARFs

B. Storage/Security of Investigational Drugs

1. Protocol specific
2. Adequate security
3. Procedures in place to protect against unauthorized prescription

C. Drug order receipts, transfers and return goods forms

1. The receipts and NCI DARFs are in agreement with NCI drug shipping records
2. All appropriate forms are kept on file.

D. Was return/transfer of drug to the NCI documented?

	YES	NO	N/A
1.			
A.	☒	☐	☐
B.	☐	☒	☐
C.	☒	☐	☐
2.			
A.			
1.	☒	☐	☐
2.	☒	☐	☐
3.	☒	☐	☐
4.	☒	☐	☐
5.	☒	☐	☐
6.	☒	☐	☐
B.			
1.	☒	☐	☐
2.	☒	☐	☐
3.	☒	☐	☐
C.			
1.	☒	☐	☐
2.	☒	☐	☐
D.	☒	☐	☐

3. RESEARCH ADMINISTRATION PROCEDURES	3.	YES	NO	N/A
A. Is there a scientific review committee within the cancer center?	A.	☒	☐	☐
B. Is approval of the scientific review committee required prior to IRB submission?	B.	☒	☐	☐
C. Are there multi-modality committees within the cancer center that determine protocol priorities?	C.	☒	☐	☐
D. Are response evaluations done by other than the treating physician and principal investigator? The treating physician initially determines the claimed response. Then any claimed tumor regression is reviewed by a central committee. The treating physician	D.	☒	☐	☐
E. Are all patients registered centrally? The zzzzzzzzzzzzzzzzzzzzzzzzzzz Office oversees the conduct of clinical trials. All patients are registered prior to study drug administration.	E.	☒	☐	☐
F. Is data management centralized? The xxxxxxxxxxxxxxxxxxxxxxx Office ensures there is adequate staffing to conduct the trial.	F.	☒	☐	☐
G. Is there a defined system for reporting serious adverse events? The research nurse and data manager are responsible to ensure all the required paperwork is completed.	G.	☒	☐	☐
H. Does the cancer center have an internal auditing system? The Quality Assurance Committee reviews accrual rates, adverse events issues, protocol deviations and provides an ongoing oversight function for the conduct	H.	☒	☐	☐
I. Are there affiliates associated with the cancer center? xxxxxxxxxxxxxxxxxxxxxxxxxxx is the only affiliate of the xxxxxxxxxxxxx Cancer Center. The same IRB serves both institutions.	I.	☒	☐	☐
J. Does the cancer center have an established auditing system for their affiliates? xxxxxxxxxxxxxxxx patients are reviewed in the same manner as any cancer center patient.	J.	☒	☐	☐

INTERVIEWS WITH PROTOCOL CHAIRS

1. Investigator: xxxxxxxxxxxxxxxx, M.D.

   Protocol: xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

   Date Approved by NCI: 0-00-99 Enrollment to Date: zz Target Accrual: 99

   Status of Study? [ ] Open [X] Closed to Enrollment [ ] Terminated [ ] On hold

   A. Is enrollment proceeding as planned?

   B. Has any anti-tumor activity been seen?

   C. Have there been any unexpected toxicities?

   D. Have there been any publications from the study?
   Work is beginning on the manuscript.

   E. Future plans: xxxxxxxxxstated the next generation of protocols is being drafted.

	YES	NO	N/A
A.	☒	☐	☐
B.	☒	☐	☐
C.	☐	☒	☐
D.	☐	☒	☐

2. Investigator: zzzzzzzzzzzzzzzz, M.D.

   Protocol: iiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiiii

   Date Approved by NCI: 00-00-99 Enrollment to Date: xx Target Accrual: 99

   Status of Study? [ ] Open [X] Closed to Enrollment [ ] Terminated [ ] On hold

   A. Is enrollment proceeding as planned?

   B. Has any anti-tumor activity been seen?

   C. Have there been any unexpected toxicities?

   D. Have there been any publications from the study?
   The manuscript is being drafted.

   E. Future plans: The next generation of protocols is being developed.

	YES	NO	N/A
A.	☒	☐	☐
B.	☒	☐	☐
C.	☐	☒	☐
D.	☐	☒	☐

4. FINDINGS AND RECOMMENDATIONS OF THE SITE VISIT TEAM

1. Therapy was not always given per protocol. At least one patient was found with therapy deviations for each of the six protocols reviewed at the site. The protocol should be followed in detail. If deviations are needed as per the clinical judgement of the treating physician, these should be clearly documented. The rationale for each modification should be documented in the medical record.

2. Nursing administration records could not be located for all the doses administered for the patients reviewed. Also, the documentation of oral medication was generally not available. All doses of study drug must be documented. The documentation should consist of the physician's order, the pharmacy dispensing record and the nursing administration record documenting what was given to the patient. Patient calendars, diaries or summary notes by the health care professional assessing compliance are all tools that can be used for documentation of oral therapy.

3. Eligibility could not be confirmed for two patients on the XXXXXXX and two patients were found to be ineligible for Protocol XXXXXXXX. The protocol must be followed in detail. All required criteria must be documented in the medical record. If an eligibility criterion is no longer felt to be clinically significant, the protocol should be formally amended.

4. Two patients on two separate protocols had missing documentation of response. The audit team disagreed with one response claim on Protocol XXXXXXXX. The protocol must be followed in detail in terms of response claims. The treating physician and principal investigator should ensure that all required information is clearly documented and their conclusion stated.

5. The process of expedited adverse event reporting should be reviewed. The audit team found one unreported event in the cases reviewed, and another event where NCI was not notified in a timely manner. It was also noted that the IRB report and the NCI notification do not always occur at the same time. This resulted in significant delays during the notification process. The NCI's and institutional guidelines should be followed in detail in terms of notification of reportable events. Reporting should be done within the timeframes specified.

6. The NCI DARFs and nursing records did not always agree on the dose of drug administered. Quality assurance measures should be put into place to ensure that the dose is consistent on both documents.

7. Two patients on Protocol XXXXXXXX were found to have inadequate consent documented. One patient spoke only Korean. The steps taken to ensure the patient fully understood the process were not documented. Another patient signed an informed consent form that did not have an IRB stamp which is required by the institution. The institutional policies for informed consent must be followed. The process of consenting non-English speaking patients must be clearly documented in the medical record.

OVERALL AUDIT OUTCOME:

Exceptional	☐
Acceptable	☐
Acceptable/Needs Corrective Action	☒
Unacceptable/Re-audit	☐

5. BRIEF SYNOPSIS OF THE EXIT INTERVIEW WITH THE PRINCIPAL INVESTIGATOR

Present at the exit interview was Drs. xxxxxx and xxxx, Mses. xxxxxxx, xxxxxx, xxxxxxx, xxxxxxx, and xxxxxxx, Mr. xxxxx, and the audit team. Drs. xxxxxx and xxxxxx presented the exit interview.

IRB: The regulatory documents were well organized. All initial approvals and amendment approvals were found. Some expedited adverse event reports were not submitted to the NCI in a timely fashion. Also, it appears that the AdEERs report and the internal adverse event report are not completed and submitted to the appropriate place at the same time. Instances were found where the AdEERs report was submitted a month after the internal form had been submitted to the IRB.

Pharmacy: The NCI DARFs were in excellent order.

XXXXiiii: The audit team often had difficulty locating the nursing administration records for Course 1. It was not always clear from the documentation when a drug was held and for what reason.

XXXXIIII: The audit team found the documentation for this study to be very good. They were easily able to find the information needed to confirm patient eligibility, study drug administration, response claims and other required parameters.

XXXXIIII: Two patients were found not to have met the eligibility criteria. Patients XX and XX had a history of peptic ulcer disease thus making them ineligible. Patient XX had a creatinine clearance of less than 60ml/min and was ineligible for this reason also.

Two patients did not speak English. The auditors could not find documentation of the steps which had been taken to ensure that these patients were fully informed about the study. Patient XX's therapy was not modified per protocol when renal insufficiency developed.

XXXXIIII: Patient XX did not receive the study drugs in the sequence defined in the protocol. Also, this patient continued on study even though progression of disease had been documented. Dr. xxxxxx recomme consideration be given to standardizing the dose modifications for standard problematic adverse events such as Grade 2 peripheral neuropathy.

XXXXIIII This protocol requires XXX be obtained to confirm patients' eligibility. This was not a part of the routine chemistry panel at the time many of these patients were treated. Therefore, eligibility could not be confirmed for these patients. A pathology report could not be located for Patient XX. Also, xxxxxxxxxx and xxxxxxxxxxxxxxxxxxxxx administration documentation was generally not found. An off st note could not be located for some patients. Patient XX died within 30 days of the last dose of study drug. An expedited adverse event report had not been filed with the NCI prior to the site visit.

XXXXIIII: One patient was reviewed. The patient started treatment on xxxxxxxx 0, 2000. They should have received 1.5mg/m^2 but received 2.2mg/m^2. The amendment with the correct dose was the version that h been IRB approved prior to the patient being treated. The patient was removed from study due to toxicity. The patient had achieved a complete response.

A tabulated summary of audit findings and case-by-case review are provided in a subsequent section of this report.

CTMS MONITOR	MONITOR'S SIGNATURE	APPROVED BY CTMS PHYSICIAN-MONITOR
xxxxxxxxxxxxxxxxxxxxxxxx	_____	_____
Deputy Project Manager, Clinical Trials Monitoring Service		xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx CTMS Principal Investigator

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NCI Site Visit to
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zzzzzz-00 2002
Prepared by the Clinical Trials Monitoring Service

Protocol #	IND Drugs	Disease	Study Chairman	Total Pts. Reg	# Selec	# Rev	# No Consent	# Inadq. Consent	# Inelig/ ? Elig	# Prot. Tx Dev	# Unver. Drug Admin.	# Miss Docu. of Response	# Respon. PI vs. Reviewer Disagree	# Serious Unreported Toxicity
XXXXIIII	xxxxxxxx	ZZZZZZZZZZZZZZZ ZZZZZZZZZZ	zzzzzzzzzzzzzzzz, MD	99	7	7	0	1	0/0	1	3	0	0	0
XXXXIIII	zzzzzzzzzz	ZZZZZZZZZZZZZZ	zzzzzzzzzzzzzzzz, MD	99	4	4	0	0	0/0	1	1	0	0	0
XXXXIIII	zzzzzzzzzz	ZZZZZZZZZZZZZZZ ZZZZZZZZZZ	zzzzzzzzzzzzzzzz, MD	99	5	5	0	2	2/1	1	0	0	0	0
XXXXIIII	zzzzzzzzzz	ZZZZZZZZZZZZZZZ ZZZZZZZZZZ	zzzzzzzzzzzzzzzz MD	99	3	3	0	0	0/0	2	0	1	1	1*
XXXXIIII	zzzzzzzzz	ZZZZZZZZZZZZZZZ ZZZZZZZZ	zzzzzzzzzzzzzzzz, M.D.	99	5	5	0	0	0/2	2	3	1	0	1
XXXXIIII	zzzzzzzz	ZZZZZZZZZZZZZZZ ZZZZZZZZZZZZZZ	zzzzzzzzzzzzzzzz, M.D.	99	1	1	0	0	0/0	1	1	0	0	0
Total				99	25	25	0	3(12%)	2/(8%) 3(12%)	8(32%)	8(32%)	2(8%)	1(4%)	2(8%)

*Delayed

Reporting